Basic Study Design

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Essential features of a clinical trial

- Test an intervention
- Controls
- Prospective
- Clinical endpoints

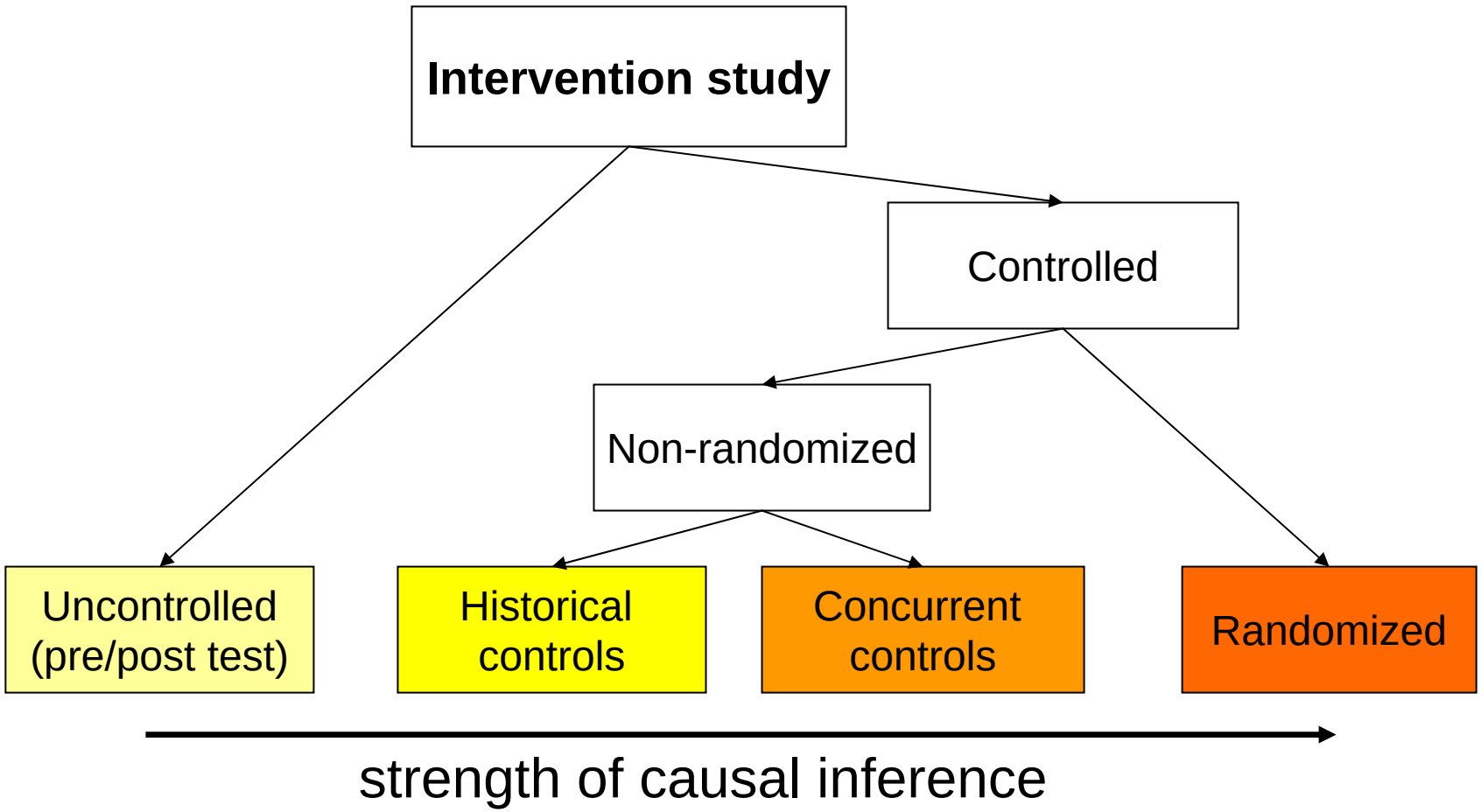
Type of Interventions

- Objective
  - prophylactic/preventive
  - diagnostic
  - therapeutic
- Method of delivery
  - (pharmacological) agents
  - devices
  - regimen
  - procedures

Phases of Clinical Trials

- Phase I
  - dose tolerance (MTD)
- Phase II
  - biologic effect or activity of treatment
  - rate of adverse events
- Phase III/IV
  - clinical effectiveness (short term)
  - long-term effect + safety (phase IV)

Basic study designs of clinical trials



Uncontrolled intervention studies

- Comparisons to controls not (yet) relevant or feasible
- Mostly used in context of pilot work
  - Proxy clinical outcomes
  - Presumed mechanism(s) of intervention as outcome

Non-randomized intervention studies

- Historical controls
  - "Control" treatment data come from data bases, existing literature, or medical records
  - Strengths
    - no one denied new treatment (more ethical)
    - Easier to recruit
    - More efficient (less costly)
  - Weaknesses
    - Poor control for bias (due to e.g., selection, changes in patient population and disease management)

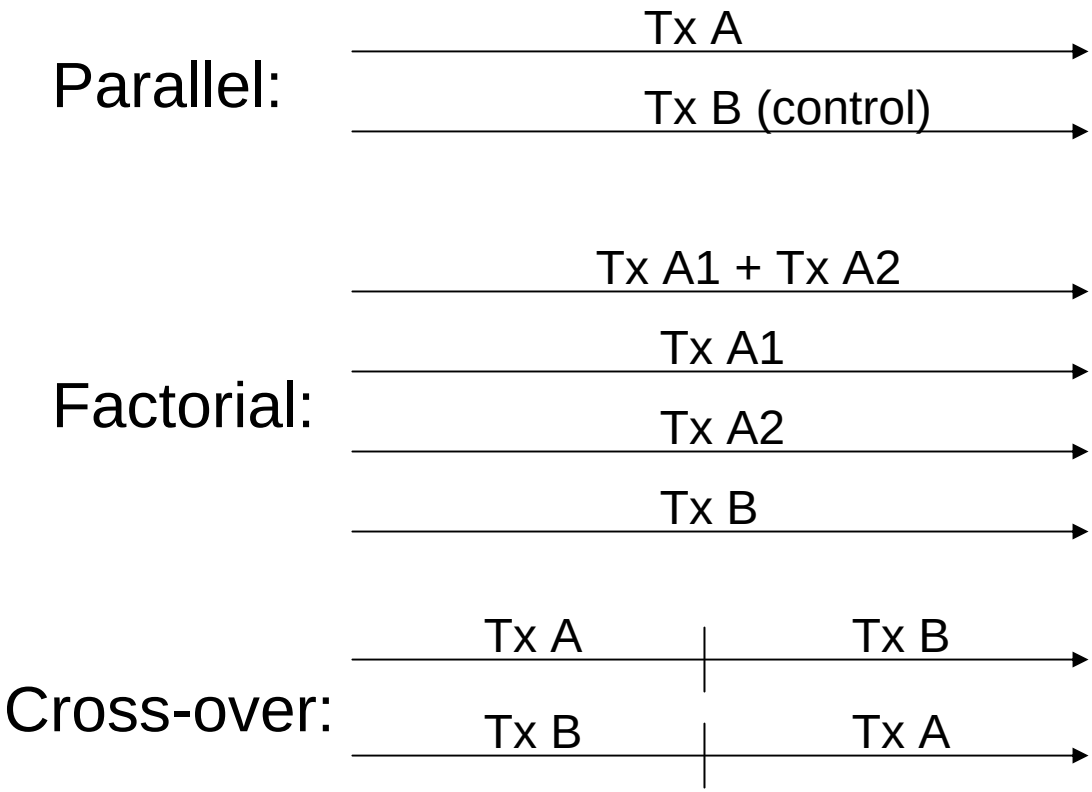
Non-randomized intervention studies

- Concurrent controls
  - Control group receives control treatment at about same time as intervention group
  - Strengths
    - Treatment is not left to chance, and may be more acceptable to participants (also favoring recruitment)
    - Cross-over of treatment can be better managed
    - Better control of differences in patient populations or in disease management
  - Weakness
    - Still potential for serious bias due to differences between patients in intervention and control groups

Types of Randomized Clinical Trials

- Parallel designs
  - 2 treatment arms
  - > 2 treatment arms
- Factorial design
  - 2 x 2 design, testing combination of $\geq$ 2 different treatments
- Cross-over design
  - Offering treatment to experimental group first, and then to control group

Basic Trial Designs



	A2	B
A1	n1	n2
B	n3	n4

Comparisons of Basic Trial Designs

	Parallel	**Factorial**	**Cross-over**
Simplicity	+	-	0
Statistical Efficiency	+	-	0
Scientific Relevance	-	+	0
Validity of Assumptions	+	0	-
Cost	+	-	+
Ethical Advantages	-	0	+

Target Population

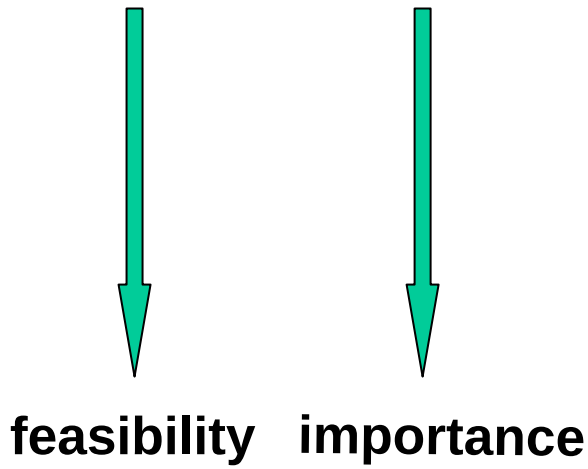
- Patients populations
  - disease-specific vs generic
  - high risk vs all
- General population (“healthy”)
  - elevated disease risk
  - not defined by disease risk

Randomization

- Simple
  - random treatment assignment per participant
- Stratification
  - randomization within clusters of participants
  - better control of potentially important prognostic factors (age, sex, race, clinical centers, regions etc.)
- Blocking
  - randomization within “blocks” of sequential participants,
  - balance between number of treatment and control participants throughout trial

Blinding (masking)

- Double blind trials
  - participant AND investigator are unaware of treatment assignment
  - “gold” standard
  - mostly for drug efficacy studies
- Single blind trial
  - participant
  - investigator/interventionist
  - outcome assessor
  - outcome event adjudicator



Follow-Up

- Duration
  - expected onset or duration of treatment benefit
  - power, or the amount of change in or number of outcome events
  - available funding
- Frequency
  - frequency of contact with participant
- Intensity
  - amount of follow-up assessment

Analysis of Clinical Trial Data

- Intention-to-treat analysis
- On-treatment analysis
- Secondary analyses
  - pre-specified
  - Exploratory
- Analysis of presumed mechanisms

What are behavioral clinical trials?

- Target of intervention is behavior
  - smoking
  - diet
  - physical activity
- Nature of intervention is behavioral
  - uses behavioral treatment modalities

Types of Behavioral Interventions

- Individual-level
  - E.g., cognitive behavior therapy (CBT)
- Group-level
  - Support groups, self-management programs
- Community-level
  - Community interventions

Achilles Heels of Behavioral Clinical Trials

- Blinding
  - awareness of treatment assignment
- Definition of control group
  - placebo, attention control, usual care?
- Randomization procedures
  - time of randomization vs beginning of treatment